IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMICUS THERAPEUTICS US, LLC and AMICUS THERAPEUTICS, INC.,	)	
Plaintiffs,	)	C.A. No. 22-1461 (CJB)
v.	)	CONSOLIDATED
TEVA PHARMACEUTICALS USA, INC. and TEVA PHARMACEUTICALS, INC,	)	
Defendants.	)	

PLAINTIFFS' OPENING POST-TRIAL BRIEF ON SECONDARY CONSIDERATIONS / OBJECTIVE INDICIA OF NON-OBVIOUSNESS

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SECONDARY CONSIDERATIONS SUPPORT NON-OBVIOUSNESS OF THE '388 AND '490 SWITCH MUTATION PATENT CLAIMS

Where present, a fact finder must "consider the objective evidence before reaching an obviousness determination" because the "objective considerations, when considered with the balance of the obviousness evidence in the record, guard as a check against hindsight bias." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Pat. Litig.*, 676 F.3d 1063, 1079 (Fed. Cir. 2012). Such objective indicia "can be the most probative evidence of nonobviousness in the record." *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1358 (Fed. Cir. 2013). Here, the objective, real-world evidence undercuts the asserted obviousness of the Switch Mutation Patents' method-of-treatment claims ('388 Patent, claims 8 and 36; and '490 Patent, claim 9).

Nexus. "[E]vidence of secondary considerations must have a 'nexus' to the claims, *i.e.*, there must be 'a legally and factually sufficient connection' between the evidence and the patented invention." *Teva Pharms. Int'l GmbH v. Eli Lilly & Co.*, 8 F.4th 1349, 1360 (Fed. Cir. 2021). Whereas Aurobindo bears the burden of proving invalidity by clear and convincing evidence, Amicus "bears the burden of showing that a nexus exists." *Id*. Amicus is "entitled to a rebuttable presumption of nexus" if Amicus shows as a matter of fact that the "objective evidence is tied to a specific product" that "embodies the claimed features, and is coextensive with them." *Id.* A "claim is not coextensive with a product that includes a 'critical' unclaimed feature." *Id.* at 1361. A patent challenger can rebut the presumption only with evidence that the objective evidence was due to unclaimed or non-novel features of the product. *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1329 (Fed. Cir. 2016).

Amicus is entitled to such a presumption here. The treatment of Fabry patients who have a switch mutation with Galafold pursuant to Galafold's FDA-approved use for such treatment (1) addressed in part the long-felt, unmet need for an alternative treatment, (2) contributed to

Amicus receiving industry awards, and (3) accomplished what another had previously tried and failed to do. Such treatment ***is*** the invention of, and embodies and is coextensive with, the Switch Mutation Claims. Pls.' Proposed Findings of Fact ("PFOF") ¶ 1. And there are no unclaimed features of treating switch-mutation patients because the patent claims are directed to that treatment. Thus, nexus is presumed. Even if nexus were not presumed, Amicus has met its burden as discussed below.

Long-Felt, But Unmet Need. It is undisputed that in 2017 (the priority date for the Switch Mutation Patents), the only available treatment for U.S. Fabry patients was Enzyme Replacement Therapy ("ERT"). *Id.* ¶¶ 2–3. Amicus provided overwhelming evidence of a long-felt, but unmet need for an alternative treatment, including among switch-mutation patients. *Id.* ¶ 4. Amicus sought FDA approval for Galafold based on there being "an unmet need" in Fabry disease for "a safe alternative to" ERT. *Id.* ¶ 5. FDA agreed and approved Galafold under an accelerated pathway because of that "unmet medical need," and granted priority review because it "would provide a significant improvement . . . over available therapies." *Id.* ¶¶ 6–7. This is unrebutted. Further, Amicus presented unrebutted evidence of ERT drawbacks to Fabry patients: (1) "infusion-related side effects as well as drug-related side effects" such as allergic reactions and "high fevers that triggered rigors and severe burning," *id.* ¶¶ 9, 12; (2) the burden of needing to have an hours-long infusion every other week, *id.* ¶ 9; (3) immunogenicity to ERT that reduces the effectiveness of ERT, *id.* ¶¶ 15–16; and (4) ERT is unable to penetrate critical organs such as the heart even though "heart disease is the number one killer in Fabry," *id.* ¶¶ 18–19.

Galafold addressed the need for Fabry patients with amenable mutations to have an alternative treatment because Galafold treatment does not come with these drawbacks of ERT. *Id.* ¶¶ 11, 14, 17, 20. Aurobindo's expert Dr. Medin admitted ERT can be immunogenic to and

burdensome for patients. *Id.* ¶¶ 10, 13, 16. He also admitted that ERT has no positive effect on heart muscle cells (cardiomyocytes), which is where Fabry patients with potentially fatal heart effects need treatment. *Id.* ¶ 19. Notwithstanding these undisputed drawbacks to ERT, Dr. Medin argued for no long-felt, but unmet need because ERT is the first-line therapy and sufficient for treatment. Trial Tr. (Day 3) at 40:6–8 (Medin). This is refuted by Dr. Medin's testimony that he is developing gene therapies as alternatives to ERT, and by Aurobindo's own efforts to commercialize a generic version of Galafold to treat Fabry patients. PFOF ¶¶ 21–22.

There is a nexus between the long-felt, but unmet need for an alternative treatment and the Amicus switch-mutation inventions because the claimed methods of treatment address the drawbacks of ERT for switch-mutation Fabry patients. *Id.* ¶ 23. That the claimed methods of treatment address the unmet need for only a subset of Fabry patients does not negate this nexus. It is well-established that "evidence of satisfying at least a portion of a long-felt but unmet need supports a finding of nonobviousness," and the patent claims need not "solve the problem for all people with" the unmet need. *UCB, Inc. v. Accord Healthcare, Inc.*, 201 F. Supp. 3d 491, 538 (D. Del. 2016) (finding non-obviousness); *see Pfizer Inc. v. Watson Pharms., Inc.*, 920 F. Supp. 2d 552, 562 (D. Del. 2013) (finding non-obviousness for rapamycin even though it "is prescribed far less frequently"). That a small number of patients had an unmet need does not render their unmet need inconsequential where, as here, personalized treatment was required given the large number of private mutations that cause Fabry. The unrebutted evidence is that Fabry is a "mortal disease," and, because Fabry is inheritable, those who suffer from or care for patients with Fabry see "morbidity and mortality all around them" and "desperately seek[] treatment opportunities." PFOF ¶ 8. The objective evidence therefore supports non-obviousness of the patent claims, even though Fabry disease is rare and migalastat treats only a subpopulation of Fabry patients.

Industry Praise. It is undisputed that Galafold received the prestigious 2018 UK Prix Galien Innovative Product Award and 2019 National Organization of Rare Disease Industry Innovation Award ("NORD Award"). *Id.* ¶ 24. The former was for "a highly innovative breakthrough therapy, a precision targeting pharmacological chaperone for the treatment of a subgroup of patients with Fabry disease who have genetically amenable mutations." *Id.* ¶ 25. And the Prix Galien Foundation recognized Amicus's "identification of patients most likely to respond [] achieved by creating a precision screening technique during the clinical trial program." *Id.* Similarly, Amicus received the NORD Award for "having a precision medicine" "targeted towards specific patients with specific mutations that would actually show the benefit from the molecule." *Id.* ¶ 26. That treatment is exactly what is in the Switch Mutation Claims here, and so a nexus exists. Aurobindo argues those patents were filed after the awards, but, as the parties agree, the Switch Mutation Patents claim priority to 2017. *Id.* ¶ 2. And courts regularly consider industry praise outside the U.S. when analyzing objective indicia. *See, e.g.*, *Genzyme Corp. v. Dr. Reddy's Lab'ys, Ltd.*, C.A. Nos. 13-1506-GMS, 13-1508-GMS, 2016 WL 2757689, at *15 (D. Del. May 11, 2016) (considering product praise for UK Prix Galien Award finalist and Spain and Greece Prix Galien Award winner).

Failure of GSK to Develop Migalastat Treatment. GSK "politely dump[ed]" its $60 million collaboration with Amicus to develop a treatment for Fabry patients in November 2013. PFOF ¶ 27. There is a nexus between GSK's exit from the collaboration and the claimed switch-mutation treatment methods because the exit shows that GSK tried, investing a large sum of money, but ultimately abandoned efforts to treat Fabry patients, including those who have a switch mutation. *Id.* ¶ 28. Contrary to Aurobindo's argument, this failure by GSK is by another, and there is no rule disqualifying the roles of third parties who collaborate with inventors. *Cf. Merck*

Serono S.A. v. Hopewell Pharma Ventures, Inc., Nos. 2025-1210, 2025-1211, 2025 WL 3030020, at *5 (Fed. Cir. Oct. 30, 2025) ("a disclosure invented by fewer than all the named inventors of a patent may be deemed a disclosure 'by another'" under pre-AIA 35 U.S.C. §§ 102(a), (e)). And while § 103 says the inventor's efforts cannot be used to ***negate*** patentability, nothing bars the Court from considering how the real-world facts refute hindsight-driven assertions of obviousness. *See* 35 U.S.C. § 103; *Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A. DE C.V.*, 865 F.3d 1348, 1356 (Fed. Cir. 2017) (relevant § 103 provision "enacted to ensure that routine experimentation does not necessarily preclude patentability").

That patients having switch mutations were not part of the clinical trials that led to FDA approval of Galafold does not destroy the nexus with GSK's failure. *Contra* Trial Tr. (Day 3) at 138:12–18, 143:12–21 (Aurobindo Closing Argument). The question for nexus is not whether FDA approval for Galafold was based on Amicus's treatment of switch-mutation patients in subsequent clinical trials after the Phase III failure. Rather, the issue is whether GSK's failure to develop the claimed inventions for treatment of switch-mutation patients with migalastat is evidence of non-obviousness. The answer is yes because GSK tried and failed to develop such treatment during its $60 million collaboration with Amicus. PFOF ¶ 28. In any event, FDA approval of Galafold could not have been conditioned on clinical trial testing of Fabry patients with switch-mutations found to be non-amenable to treatment under the R&D HEK Assay. *See id.* ¶ 29. It would have been unethical for Amicus to enroll switch-mutation patients in the clinical trials because the prior art taught that those patients were not amenable to migalastat treatment, as Amicus's communications with FDA made clear. *Id.* Only after Amicus's GLP HEK Assay showed that mutations switched from amenable to non-amenable, and vice versa, did FDA approve Galafold for use to treat switch-mutation patients. *Id.* ¶ 30.

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November 5, 2025

CERTIFICATE OF SERVICE

I hereby certify that on November 5, 2025, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on November 5, 2025, upon the following in the manner indicated:

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